C1 --This application is a continuation of U.S. Patent Application No. 09/138,958, filed August 24, 1998, now U.S. Patent No. 6,306,643, which is incorporated herein by reference.--

Please replace the paragraph beginning on page 9, line 7 with the following rewritten paragraph:

C2 --Fig. 4A. Fluorescence images of cooperative vs. non-cooperative hybridization to paired probe arrays. The design of the array is shown in Fig. 3. Unambiguous hybridization to the double perfect match probe pair is shown for four different linked sequence pairs (10g–27c, 10c–27t, 10c–27g, and 10g–27t from top of left hand column). Hybridization images of the corresponding unlinked targets are shown in the adjacent right hand column.--

Please replace the paragraph beginning on page 9, line 16 with the following rewritten paragraph:

C3 --Fig. 4B 50:50 mixtures of (10c–27t and 10g–27c) and (10g–27t and 10c–27c) are shown in the two panels of the left hand column. Although the two experiments have targets that are identical in sequence composition, the pairing is different. This is clearly detected in the experiment, which allows the pairings (linkages) to be determined in each case. The bottom panel in the right hand column shows a hybridization image of (10c, 10g, 27c, and 27t). The sequence composition is identical to the two lower panels of the left hand column. However, in this case the individual targets are unlinked, and hence no cooperative effect is observed.--

Please replace the paragraph beginning on page 32, line 11 with the following rewritten paragraph:

C4 --Hybridizations were performed as described in Table 1. Different mixtures of DNA target complementary to Probe 1 and Probe 2 were used to investigate the extra stability of the paired hybridization (Fig. 4A). The fluorescence intensity of the linked targets was always greater than 40x the intensity of their unlinked counterparts. The intensities of the linked targets in the regions where they matched both paired probes were 2-3x the sum of the intensities where

they matched just Probe 1 or Probe 2. For the unlinked targets, the intensities in the regions where the targets matched both paired probes was 15-35% less than the sum of the regions where they matched Probe 1 or Probe 2. This 15-35% loss of signal may be due to crowding effects at the surface, since almost twice as much target is present in the regions where the targets match both probes. The discrimination ratio between the correct calls and single base changes was also markedly better with the linked targets. These results demonstrate the cooperative hybridization of linked target sequences to paired probes. In every case, the linkage or independence of N1 and N2 was clearly distinguished, and the variable bases at N1 and N2 were correctly determined in the physically linked targets.--

Please replace the paragraph beginning on page 32, line 34 with the following rewritten paragraph:

--Assignment of linkage in a heterozygous mixture. To determine if hybridization to paired probe arrays could be used to assign linkage directly in complex heterozygotes, two further experiments were conducted. In each case, equimolar mixtures of two linked targets were hybridized to a 9-mer paired probe array. In the first experiment, the mixture consisted of 10c–27t and 10g–27c. In the second experiment, the mixture was of 10g–27t and 10c–27c. Although the two experiments have targets that are identical in sequence composition, the pairing is different. The results are shown in the left-hand bottom two panels of Fig. 4A. In each mixture, it was straightforward to assign linkage. In each case, the linked sequences are clearly discriminated from the other possible arrangements (e.g. c–c, g–t vs. g–c, c–t). Even though the probes in the four array positions c–c, c–t, g–c, g–t are complementary to equimolar amounts of target in the hybridization mixture, there is significantly more signal where the two probes are perfectly complementary to the same target molecule (1.4-7 x intensity). Furthermore, the control hybridization, in which unlinked targets have the same sequence composition as the linked targets, shows lower signal and no evidence of cooperativity. These results show that paired probe arrays can be used to assign linkage in mixtures containing two different multiply polymorphic alleles.--